

Effective Health Care

Bulletin on the effectiveness
of health service interventions
for decision makers

This bulletin summarises
the research evidence
that informed the
guidance 'Improving
Outcomes in Head and
Neck Cancers'



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Management of head and neck cancers

- Over the next few years, assessment and treatment services for patients with head and neck cancers will become increasingly concentrated in cancer centres serving populations of over a million.
- Multidisciplinary teams (MDTs) will be central to the service, each managing at least 100 new cases of upper aerodigestive tract cancer per annum. They will be responsible for assessment, treatment planning and management of every patient. Specialised teams will deal with patients with thyroid cancer, and with those with rare or particularly challenging conditions such as salivary gland and skull base tumours.
- Arrangements for referral at each stage of the patient's cancer journey should be streamlined. Diagnostic clinics should be established for patients with neck lumps.
- A wide range of support services should be provided. Clinical nurse specialists, speech and language therapists, dietitians and restorative dentists play crucial roles but a variety of other therapists are also required, from the pre-treatment assessment period until rehabilitation is complete.
- Co-ordinated Local Support Teams should be established to provide long-term support and rehabilitation for patients in the community. These teams will work closely with every level of the service, from primary care teams to the specialist MDT.
- MDTs should take responsibility for ensuring that accurate and complete data on disease stage, management and outcomes are recorded. Information collection and audit are crucial to improving services and must be adequately supported.
- Research into the effectiveness of management – including assessment, treatment, delivery of services and rehabilitation – urgently requires development and expansion. Multi-centre clinical trials should be encouraged and supported.

A. Background

A.1. Incidence and mortality

There are over 30 specific sites in the head and neck cancers group. Cancer of each particular site is relatively uncommon (Tables 1 and 2), however the group as a whole accounts for over 8,000 cases and 2,700 deaths per year in England and Wales.

The majority of these cancers arise from the surface layers of the upper aerodigestive tract (UAT): the mouth, lip and tongue (oral cavity), the upper part of the throat and respiratory system (pharynx), and the voice-box (larynx). Other UAT sites include the salivary glands, nose, sinuses and middle ear, but these cancers are relatively rare; cancers that originate in the nerves and bone of the head and neck are even rarer.

This bulletin also deals with cancer of the thyroid, a gland in the neck that produces hormones that regulate metabolism. Like cancers of other sites in the head and neck, it is uncommon. In most

other respects, thyroid cancers are unlike UAT cancers, but the services required for patients overlap.

Survival rates: The prognosis for individual patients depends heavily on the stage of the disease and co-morbidities. Disease stage can be described most precisely in terms of the size of the initial tumour (T), the extent of lymph node involvement (N), and the presence or absence of metastatic spread (M). The system often used in the UK ranges from Stage I (early disease) to IV (metastatic). Figures for stage at diagnosis and survival rates for UAT cancers for the South and West of England are given in Table 3, below. The relationship between this system and TNM stage for each cancer site is complex, but details are given in the document from which these figures were derived.³

A.2 Risk factors

Cancers of the UAT: Most UAT cancers are related to alcohol and tobacco consumption, which together probably account for three-quarters of cases.⁴ Cigarette

smoking is associated with increased risk of all of the more common forms of UAT cancer; the risk among cigarette smokers may be ten or more times higher than that for non-smokers. Pipe or cigar smoking is associated with an even higher excess risk of oral cancer.⁵ Chewing tobacco – with or without areca (betel) nut – is strongly linked with oral and pharyngeal cancer, as well as to some extent with cancer of the larynx and the thyroid.^{6,7}

High alcohol consumption and smoking have synergistic or multiplicative effects on the risk of head and neck cancer. For heavy drinkers who are also heavy smokers, the risk of oral cancer is over 35 times that for those who neither smoke nor drink, and a similar pattern is found with cancer of the larynx.^{4,8} Alcohol consumption is a particularly important risk factor for cancers of the mouth and pharynx and, to a lesser degree, for cancer of the larynx. Consuming 100g of alcohol or more per day (about twelve units – six pints of beer or twelve measures of wine or spirits) multiplies the risk of developing oral cancer at least six-fold, after adjustment for tobacco use; the more alcohol consumed, the greater the risk.⁹

Diet also affects the risk of cancers of the oral cavity, pharynx and larynx; as with many other forms of cancer, frequent consumption of fruit and vegetables is associated with reduced risk. Poor diet is often associated with heavy smoking and alcohol use, and the malnutrition that can result exacerbates the risk of cancer.

Thyroid cancer: A history of radiation exposure to the neck area is associated with increased risk of thyroid cancer, often after a delay of well over a decade; some cases can be traced to radiation treatment in childhood. Both deficiency and excess of dietary iodine are associated with increased risk.¹⁰ Other predisposing factors include prolonged stimulation with thyroid stimulating hormone (which can be due to chronic iodine deficiency), chronic lymphocytic thyroiditis (lymphoma), and genetic factors

Table 1 Registrations, incidences and deaths, England 2000¹

Cancer site	ICD10 code	Number of registrations	Number of registrations		Deaths	Mortality: crude rate per 100,000	
			Men	Women		Men	Women
Mouth, lip & oral cavity	C00-06	2329	5.9	3.7	782	1.8	1.3
Salivary glands	C07-8	422	1.0	0.8	138	0.3	0.2
Pharynx (throat)	C09-14	1339	4.0	1.6	617	1.7	0.8
Nasal cavity, ear & sinuses	C30-31	352	0.8	0.6	110	0.3	0.2
Larynx (voice-box)	C32	1903	6.6	1.3	655	2.1	0.5
Thyroid	C73	1131	1.3	3.3	251	0.3	0.7

Table 2 Registrations, incidences and deaths, Wales 2000²

Cancer site	ICD10 code	Number of registrations	Number of registrations		Deaths	Mortality: crude rate per 100,000	
			Men	Women		Men	Women
Mouth, lip & oral cavity	C00-06	166	7.1	4.4	45	1.8	1.3
Salivary glands	C07-8	47	1.6	1.6	8	0.3	0.3
Pharynx (throat)	C09-14	90	4.7	1.6	43	1.9	1.1
Nasal cavity, ear & sinuses	C30-31	21	0.9	0.5	7	0.4	0.1
Larynx (voice-box)	C32	147	9.0	1.4	54	3.0	0.8
Thyroid	C73	57	1.3	2.6	8	0.1	0.4

Table 3 Cancer stage and survival in the South and West of England, 1999-2000³

Stage	Two-year survival, crude rate (all sites)	Cancer site (% of cases at each stage at diagnosis)				
		Larynx n=190	Oral n=241	Pharynx n=161	Salivary gland n=56	Other n=79
I early disease	89.7%	34	21	6	13	12
II locally advanced	71.8%	27	16	13	17	8
III tumour in lymph nodes	57.6%	17	15	22	7	8
IV metastatic	48.6%	15	34	50	28	47
Unknown	69.8%	7	11	9	35	25

(linked with medullary thyroid cancer). Women are more than twice as likely as men to develop thyroid cancer.

A.3 Bulletin context

The National Institute for Clinical Excellence has now published guidance on head and neck cancer services.¹¹ As part of the guidance development process, review questions were generated (for full details see Appendix 2 of the manual). These questions do not address every aspect of management but those considered key to inform the production of the guidance. Systematic reviews of the research evidence were undertaken by the Centre for Reviews and Dissemination (CRD) to answer these questions. A summary of these reviews has also been published.¹² The guidance documents, including a patient summary, can be obtained via the NICE website (www.nice.nhs.uk). The key recommendations from the guidance are given in Section B below. This bulletin summarises the research evidence that informed the guidance.

B. Key recommendations

In the guidance manual,¹¹ the following key recommendations were identified as priorities for the NHS, which, if implemented, would make a major contribution to improving outcomes in head and neck cancers.

- Services for patients with head and neck cancers should be commissioned at the cancer network level. Over the next few years, assessment and treatment services will become increasingly concentrated in cancer centres serving populations of over a million.
- MDTs with a wide range of specialists will be central to the service, each managing at least 100 new cases of UAT cancer per annum. They will be responsible for assessment, treatment planning and management of every patient. Specialised teams will deal with patients with thyroid cancer,

and with those with rare or particularly challenging conditions such as salivary gland and skull base tumours.

- Arrangements for referral at each stage of the patient's cancer journey should be streamlined. Diagnostic clinics should be established for patients with neck lumps.
- A wide range of support services should be provided. Clinical nurse specialists, speech and language therapists, dietitians and restorative dentists play crucial roles but a variety of other therapists are also required, from the pre-treatment assessment period until rehabilitation is complete.
- Co-ordinated Local Support Teams should be established to provide long-term support and rehabilitation for patients in the community. These teams will work closely with every level of the service, from primary care teams to the specialist MDT.
- MDTs should take responsibility for ensuring that accurate and complete data on disease stage, management and outcomes are recorded. Information collection and audit are crucial to improving services and must be adequately supported.
- Research into the effectiveness of management – including assessment, treatment, delivery of services and rehabilitation – urgently requires development and expansion. Multi-centre clinical trials should be encouraged and supported.

C. Referral

Diagnosis and assessment of patients with possible head and neck cancers requires a sequence of activities that take place at different levels of the service. When patients first present to their GP with symptoms, it is usually not obvious whether the patient has cancer. Most will first be referred to a local hospital ENT or maxillofacial clinic, where cancer will be found or strongly suspected in a small minority of cases. These patients require onward referral for further assessment, normally in a tertiary centre.

Because head and neck cancer is relatively rare, the average GP would expect to see a new case only every six years; an otolaryngologist (ENT specialist) or maxillofacial surgeon working in a district general hospital would expect to see one new case every six weeks. Some forms of oral cancer may be initially diagnosed by dentists, who are trained to carry out a comprehensive examination of all areas of oral mucosa (gum and interior of the mouth) when patients attend for dental care. Pharmacists may also be able to alert customers to the need for investigation, for example if they frequently buy treatments for mouth ulcers or are hoarse for a month or more.

C.1 Early detection of malignancy

Two observational studies provide evidence that patients whose cancers are detected later require more extensive treatment and experience poorer outcomes.

An interview-based Brazilian study that investigated delays in the referral pathway showed that the majority (58%) of delays were caused by patients delaying consultation with health professionals.¹³ However, health professionals were solely responsible for delay in 13% of cases and responsible for at least some of the delay in a further 11% of cases. The study assessed whether patients who had experienced delays were more likely to be diagnosed with late stage disease than those patients who had experienced no delays. The assessment found that patients who did not delay in reporting symptoms to a professional were approximately half as likely to present with late stage disease. There was a dramatic increase in hospital costs with more advanced disease.

An audit conducted in the West of Scotland region found that late stage presentation was common.¹⁴ Patients presenting with Stage 1 disease fared significantly better than those presenting with all other stages in terms of post-therapy disease-free interval. They also had a significantly better overall survival rate than patients presenting with Stage III or IV disease.

C.2 Raising professionals' awareness of the existence of head and neck cancers

A brief, multi-component educational intervention designed to teach health care professionals about the oral sites at risk, aetiological factors and early signs and symptoms of oral and pharyngeal cancers, and screening techniques was assessed in a US study.¹⁵ Doctors, allied health professionals and medical students demonstrated increases in knowledge levels while the dentists and nurses participating failed to demonstrate increased levels of knowledge. Dentists were the only group who did not feel they needed additional training following the intervention.

This study suggests that an educational intervention may be beneficial but the professional grouping at which it is aimed may be a factor in its usefulness. The failure of dentists and nurses to increase their levels of knowledge may be related to the level at which the intervention was pitched or its format. No patient outcomes were measured.

C.3 Opportunistic screening

A UK study of the feasibility of systematic examination of the oral mucosa by dentists concluded that this could be carried out as part of a routine dental inspection.¹⁶ A total of 1,949 employees who benefited from employer-sourced dental healthcare were invited to attend a mucosal inspection session as part of their routine dental check-up; 1,947 employees agreed and were seen. One hundred and fifty-five patients (8%) were found to have oral lesions. Of these, 151 were diagnosed as having innocent or benign conditions, there were two cases of tobacco-associated leukoplakia, one case of reticular lichen planus and one case of squamous cell carcinoma. However, this is a specific sub-population and was not in an NHS setting.

C.4 Rapid access to a specialist/dedicated diagnostic clinic

Persistent hoarseness: Two studies examined 'persistent hoarseness' or 'husky voice' clinics. A well-conducted study of 271 patients who attended a direct referral, immediate-access hoarse

voice clinic found that the average waiting time for attendance at the clinic was three weeks.¹⁷ Thirty-nine (14%) patients were found to have suspicious lesions on indirect laryngoscopy at the clinic and were admitted for direct laryngoscopy and biopsy under anaesthetic. Ten of these 39 patients were diagnosed with cancer of the larynx, three were diagnosed with dysplasia and one with cancer of the tongue.

An audit of 34 patients referred to a pilot 'husky voice' clinic with agreed referral protocols reported that 94% of patients were seen within five working days and five referrals (15%) were inappropriate.¹⁸ One case of cancer was reported.

Lump and bump clinics: Three studies were found which examined the effects of lump and bump clinics. One controlled study compared two cohorts of 50 patients referred to a 'lump and bump' clinic and found that the mean time between the date of the referral letter and the outpatient appointment increased from 13.8 days to 25.4 days after implementation of the two-week wait initiative.¹⁹ The pick-up rate for malignancy was 4% in patients referred via the two-week wait initiative and 14% for non-two-week wait 'lump and bump' clinic patients. However, the possible influence of other factors occurring at the same time as the implementation of the two-week wait initiative reduces the reliability of the results presented. An audit and re-audit of a 'one-stop' head and neck lump clinic with the provision of immediate fine needle aspiration cytology (FNAC) assessment and reporting found that over two-thirds of 245 patients referred to the clinic were managed during only one visit each.^{20,21} The accuracy of immediate FNAC was 94%. The mean number of days patients waited to be seen in the clinic was 17 in the first audit and 21 in the re-audit and the mean waiting time at the clinic was about an hour in both audits.

Of 100 patients referred to a direct referral clinic for a neck mass, for which practitioners were advised of the appropriate route of referral, 46 were referred with enlarged

lymph nodes, 21 for thyroid swelling and 17 for salivary gland swellings.²² Two referrals were considered to be inappropriate. Of the patients referred with enlarged lymph nodes, 10 were found to have squamous cell carcinoma and three had lymphoma. Four thyroid swellings and two salivary gland swellings were malignant.

D. Structure of services

D.1 Role of multidisciplinary teams (MDTs)

Professionals seem to value the opportunities afforded by the MDT system.^{23,24} Where appropriate procedures are in place, good clinical outcomes may be promoted by management by a MDT.²⁵

D.2 Types of staff involved

It is generally accepted that a wide range of specialist support services should be provided. Although there is consensus that speech and language therapists, dietitians, specialist nurses and restorative dentists can play crucial roles, the limited evidence found in this area was of poor quality and definitive conclusions cannot be drawn.

Speech and language therapists (SLTs).

Data from three research studies²⁶⁻²⁸ which investigated the opinions of patients who had undergone a laryngectomy suggest that patients feel they benefit from the opportunity to see SLTs both before and after surgery. The findings are limited by the weak designs used and poor reporting of the SLT interventions in the studies. The age of the studies is also of concern.

Dietitians. Two studies were found which suggest that interventions which may be advised by dietitians or nutritionists have beneficial effects on patients.^{29,30} The paucity of evidence and the low validity of the methods used in the research studies mean that this conclusion is only tentative.

Specialist nurses. Specialist nursing care has not been extensively studied in comparative studies. The evidence located was economic in nature but did suggest

benefits of sub-specialisation in nursing.³¹ No definitive conclusions may be drawn.

D.3 Location of services

An extensive UK focus-group study found that patients and relatives were concerned about mixed sex and mixed speciality wards.^{23,24} They felt strongly that head and neck cancers should be managed on a dedicated ward or area within a ward, with adequate privacy and specialist nursing skills. Professionals supported the proposal in theory, but some had reservations about over-specialisation and the loss of variety in their work.

D.4 Volume and outcomes

Clinician volume. One study examined a series of 5,860 patients who underwent thyroid surgical procedures between 1991 and 1996.³² The complication rate for non-unilateral subtotal thyroidectomy procedures was significantly higher in patients treated by surgeons who operated on fewer than ten patients than in those whose surgeons operated on more than 100 patients in the study period. The length of hospital stay was lower in patients treated by surgeons who operated on more than 100 patients than any of the other volume categories for all surgical procedures; the difference was statistically significant in almost every category.

Hospital volume. In a retrospective survey of Scottish cancer registry data, the effects of hospital volume were examined by comparing the largest provider with the remaining providers.¹⁴ The high-volume provider saw 124 (60%) of the total 206 patients. The remaining 40% of patients were treated in 13 units. Patients treated at the high-volume provider had a significantly lower risk of death and a significantly lower risk of recurrence. This association between treatment centre and survival or risk of recurrence was not apparent when the treatment strategy was included as a covariate. This suggests that the improvement in outcomes for patients seen in the high-volume provider may, in part at least, be related to the choice of treatments offered.

E. Initial investigation and diagnosis

Initial investigation is usually by close inspection of the affected area. When the lesion is inaccessible, endoscopy (pharyngolaryngoscopy) – usually using a fibre-optic device inserted into the pharynx and/or larynx – is essential. A definite diagnosis of cancer requires the removal of a small quantity of tissue for microscopic examination, using biopsy when the lesion is on the lining of the mouth or airway, or fine needle aspiration for neck lumps.

E.1 Fine needle aspiration cytology in patients with symptoms suggestive of thyroid cancer

In a study investigating whether core needle biopsy (CNB) provides additional information over fine needle aspiration biopsy (FNAB), 29 patients diagnosed as having thyroid nodules on ultrasound had both index tests, as well as a definitive histological diagnosis after surgery.³³ However, 13 CNBs did not provide sufficient material for diagnosis, so the respective accuracy of the tests is only reported for 16 patients. The accuracy of FNAB was 94% compared with 100% for CNB. The sensitivity of FNAB was 86% and the specificity was 100%. The sensitivity and specificity of CNB were both 100%. The fact that diagnostic conclusions could only be drawn from 55% of CNBs, in contrast to 100% of FNABs, suggests that the overall efficacy of FNAB is probably superior. However, the risk of false negatives needs to be acknowledged. Due to the small sample size this study should be regarded as suggestive rather than definitive.

E.2 Written information

A Canadian study investigated recall rates among head and neck cancer patients of a combined oral and written intervention.³⁴ The intervention consisted of an illustrated pamphlet and an oral explanation of the possible complications and risks of surgery.

When compared to patients who only received the oral explanation, the patients who also received the pamphlet were statistically significantly more likely to recall the potential complications of the procedure (mean recall rate 50% versus 30%; p < 0.001).

This study was described by its authors as being a randomised controlled trial (RCT) but they did not report the method of randomisation, nor whether blinding of the outcome assessors was used. Patient outcomes other than ability to recall what had been told to them were not measured. These factors may affect the generalisability of the results but the marked differences in the recall rates could still be considered supportive of written information packages.

Three studies from the UK also suggest that written information may be helpful to patients.³⁵⁻³⁷

Written information is sometimes used in isolation, but when it is used in combination with other means of communication the relative effects of the various concurrent interventions cannot be identified. Nevertheless, the evidence suggests that written information has a role to play in this setting.

F. Pre-treatment assessment and management

Various forms of imaging may be used to stage head and neck cancer; that is, to discover the size and extent of the primary tumour and to find out if it has spread to nearby lymph nodes or to more distant sites (metastases). In practice, staging at the time of initial assessment may not be accurate and the speed at which any particular tumour may grow is not known, so predicting prognosis is difficult. Also, the patient's general health has a marked effect on survival.

F.1 Effectiveness of imaging in assessing chest involvement

Two studies compared the effectiveness of X-rays with CT for

screening for tumours in the chest in patients with head and neck cancers.^{38,39} Both found that CT was significantly more sensitive, but the specificity of X-ray imaging was slightly higher. However, given the methodological limitations in both of the studies, the results should be interpreted with caution.

F.2 Nutritional assessment

Two studies suggest that early nutritional assessment and intervention, including percutaneous gastrostomy (PEG) insertion, appears to be effective in preventing weight loss and dehydration in head and neck cancer patients undergoing radiotherapy.^{30,40}

F.3 Dental assessment

The results of four studies with relatively large sample sizes suggest that dental assessment prior to radiotherapy for head and neck cancer is beneficial. The majority of patients in each study required dental treatment before the commencement of radiotherapy.⁴¹⁻⁴⁴

Radiotherapy can cause adverse effects on the jaw, teeth and oral cavity, such that specialised dental management may also be required after treatment.⁴⁵

F.4 Shared decision-making

Information from one qualitative study of head and neck cancer patients and their professional carers suggests that patients often want to be involved in deciding the course of their treatment but many feel excluded from the decision-making process.^{23,24} Doctors differed in the degree to which they believed patients should be involved in decision-making, but felt that they often did not provide patients with the full range of options or the information required to decide between different treatments.

F.5 Availability of psychosocial care

Several studies were found which investigated the effects of psychosocial care.⁴⁶⁻⁵¹ While the types of psychosocial interventions and methods used varied between the studies found, most of the research suggested that

psychosocial care was beneficial to patients with head and neck cancer. This was true of all of the experimental studies located. However, the methodological flaws and the lack of reliability inherent in the methods used mean that the findings are at best suggestive.

F.6 Availability of counselling

Information from one qualitative study of head and neck cancer patients suggests that some patients wish to receive counselling but that they are not often offered this facility.^{23,24} Patients appeared to want someone with whom to discuss their problems, rather than someone who would offer solutions without listening closely to them.

F.7 Provision of a patient visitor

It appears from five attitudinal surveys that patients who have undergone laryngectomy are keen to have contact with rehabilitated patients who have previously undergone the same procedures.^{23,24,26-28,35} The individual preferences of the patient should be taken into account in deciding the timing of the meeting.

F.8 Smoking cessation programmes

In a RCT, 186 newly diagnosed head and neck cancer patients (88% of whom were current smokers) were randomised to either a 12-month smoking cessation programme or usual care advice.^{52,53} 70% of patients followed-up for a year were continuous abstainers, but there were no significant differences between the groups. No adverse effects were reported. Given the lack of methodological details reported, the results should be interpreted with caution.

G. Primary treatment

Most head and neck cancers are treated with surgery or radiotherapy or a combination of both. Chemotherapy alone is rarely appropriate for these forms of cancer, but chemotherapeutic

agents are sometimes used to enhance the effects of radiotherapy; this is known as chemoradiation. Reconstructive surgery and specialised dentistry are often needed. Patients need considerable help and support with nutrition and communication, both during and after primary treatment.

Thyroid cancers are usually treated by surgical removal of the thyroid gland. Radioiodine treatment, which requires special protected rooms, may be used to destroy residual disease. Endocrinologists play important roles in the management of patients treated for thyroid cancer, who require thyroid hormone replacement therapy and monitoring for the rest of their lives. The cancer can recur many years after primary treatment, but most patients will remain free from it.

G.1 Relative efficacies of treatment modalities

The evidence suggests that concomitant chemotherapy increases survival and loco-regional control for patients with head and neck cancer, but no statistically significant survival benefit has been demonstrated with adjuvant or neoadjuvant chemotherapy (other than in a subgroup analysis which detected significantly improved survival with neoadjuvant chemotherapy using 5-fluorouracil in combination with either cisplatin or carboplatin).⁵⁴⁻⁵⁸ The evidence relating to specific agents is contradictory with regard to the efficacy of platinum-based chemoradiation.

Patients with newly diagnosed locally advanced nasopharyngeal cancer treated with chemoradiation had significantly higher rates of disease-free survival than patients treated with radiotherapy alone.⁵⁹ This was found for neoadjuvant chemotherapy, concurrent chemotherapy and concurrent adjuvant chemotherapy. The use of concomitant chemotherapy has been found to significantly enhance both acute and late radiation morbidity effects.

In a large trial of patients with newly diagnosed, locally advanced

head and neck cancer, two-year loco-regional control rates were higher in patients receiving accelerated radiotherapy with a concomitant boost or hyperfractionated radiotherapy than those receiving accelerated radiotherapy with a split course or conventional treatment. However, overall survival was not statistically significantly different between the arms.^{60,61} Trials have reported increased acute toxicity with accelerated radiotherapy compared with conventional radiotherapy. Hyperfractionated radiotherapy has been associated with increased mucosal and skin toxicity compared with conventional radiotherapy. A reduction in the risk of death has been found in patients receiving hyperfractionated radiotherapy over those receiving conventional radiotherapy in one review;⁶² patients treated with hyperfractionation were less likely to respond incompletely to treatment or to suffer local recurrence.

In a larynx preservation trial patients allocated to a concomitant chemotherapy and radiotherapy group had significantly greater loco-regional control and larynx preservation than patients allocated to neoadjuvant chemotherapy or radiotherapy alone. In another study patients who had been randomised to neoadjuvant chemotherapy in combination with radiotherapy scored significantly better in mental health and pain assessments than patients who had been randomised to surgery and radiotherapy.⁵⁶

G.2 Adherence to a treatment protocol and specified timescales

The results of two cohort studies suggest that the introduction of a clinical care pathway may reduce the average length of hospital stay and total costs.^{63,64}

G.3 Adherence to specified radiotherapy timescales

A systematic review of individual patient data found that compliance with the prescribed radiation therapy schedule was relatively poor, with an agreement between overall and ideal treatment time in

only 30% of cases; 7% completed treatment sooner than planned.⁶⁵ Clinical outcomes were not evaluated.

A reanalysis of data from two RCTs including 828 patients found that only 278 patients had received radiotherapy exactly as per their protocol.⁶⁶ The analysis identified a time factor of 0.8Gy per day as the extra dose required to counteract the reduction in tumour control probability with extension of the treatment time. Despite the theoretical nature of the calculations, the results appear to be valid. Again, clinical outcomes were not evaluated.

Four other studies found that prolonged overall treatment time led to worse loco-regional control and disease-free survival.⁶⁷⁻⁷⁰ In the reanalysis of data from the conventional arm of the CHART trial,⁶⁸ patients receiving radiotherapy for 49 days or more (mean 51.5 days) had an increase in relative risk of death of 19% compared with patients receiving radiotherapy for 48 days or fewer (mean 45.7 days). When adjusted for factors collected before treatment, the increase in risk of death was 9%. In the case-control study,⁷⁰ 12% of patients in the continuous course radiotherapy group and 17% of patients in the split course radiotherapy group had prolonged overall treatment time (treatment that extended more than one week beyond the schedule). Each day of interruption of treatment was found to increase the hazard rate for reduced loco-regional control by 3.3% and disease-free survival by 2.9%.

G.4 Delays in initiating radiotherapy

A systematic review was found which included four RCTs and 42 case series, of which 12 case series related to head and neck cancer.⁷¹ Of these, five related to primary radiotherapy ($n=2,427$) and seven to post-operative radiotherapy ($n=851$).

The five studies of delays in initiating treatment in patients being treated primarily with radiotherapy suggested that such delays may adversely affect loco-regional control rates. However,

the findings were contradictory. One of these studies suggested that long-term survival was improved for those treated sooner.

Seven studies of delays in initiating treatment in patients being treated with postoperative radiotherapy indicated that delays in initiating radiotherapy adversely affect loco-regional control rates. Two of these studies reported contradictory findings relating to long-term survival.

Insufficient information was presented in the review to identify an appropriate time frame for either the period from diagnosis to treatment initiation or from surgery to initiation of radiotherapy.

G.5 Interventions for the prevention and/or treatment of mucositis

The evidence relating to head and neck cancer patients suggests that the use of prophylactic narrow-spectrum antibiotics is beneficial for preventing severe oral mucositis in patients receiving radiotherapy.⁷² Amifostine was beneficial in patients undergoing chemoradiotherapy; it did not affect the anti-tumour effectiveness of radiotherapy and it rarely produced severe adverse effects. It was not found to significantly benefit head and neck cancer patients undergoing radiotherapy without concurrent chemotherapy.⁷³

In cancer patients receiving chemotherapy or radiotherapy treatment, ice chips and GM-CSF prevented mucositis and antibiotic paste or pastille and amifostine provided moderate and minimal benefits in preventing mucositis, respectively.⁷⁴ Hydrolytic enzymes reduced the severity of mucositis, as did allopurinal, although the evidence for the latter was unreliable.

G.6 Interventions to reduce the severity of the symptoms of xerostomia

Three reviews were found in which pilocarpine hydrochloride and amifostine were found to significantly reduce the effects of radiation-induced xerostomia (dry mouth) in patients with head and

neck cancer.^{73,75,76} Adverse effects of both agents were common, but not severe or life threatening.

However, these conclusions should be interpreted with caution owing to the lack of information about the methods used in two of the reviews and possible heterogeneity between included studies.

H. After-care and rehabilitation

Living with the effects of head and neck cancer can be difficult for both patients and carers. Radiotherapy can be debilitating, with many persistent side-effects, and people can have difficulties with speaking, chewing and swallowing, which can add to problems with nutrition. Those who have undergone laryngectomy (surgical removal of the larynx) must permanently cope with breathing through an opening in the neck (stoma) and with dealing with any secretions coughed out through the stoma, as the airway is completely separated from the gullet (pharynx and oesophagus). These patients need to learn to communicate in a new way. Those who undergo oral and facial surgery may face difficulties with eating, drinking and talking, and may have to learn to live with facial disfigurement. Such patients need specialised support from a variety of professionals, particularly specialist nurses, speech and language therapists, and dietitians.

H.1 Rehabilitation services

The review did not locate any well-designed studies of the effectiveness of speech and language therapy, as provided in the NHS. The majority of identified studies were retrospective in nature, with potential biases and a lack of detail on the content of speech and language therapy interventions.^{26,77-87} However, questionnaire-based studies and case series reports support the view that speech and language therapy is beneficial in the rehabilitation of patients with head and neck cancer. One case

series study of art therapy was identified which suggested that there may be a role for art therapy for patients with laryngeal cancer.⁸⁸ However this result was based on the opinions of the therapist rather than patients.

H.2 Osseointegrated implants

A number of studies were found which investigated the outcomes of dental and facial bone restoration using prostheses retained by osseointegrated implants.⁸⁹⁻¹⁰¹ In view of the potential biases in these studies, no conclusions on the effectiveness of the interventions reported can be regarded as reliable. It appears that the probability of osseointegration may be reduced in patients who have had radiotherapy. Some evidence exists that suggests that hyperbaric oxygen therapy may ameliorate the effect of radiotherapy on osseointegration. While treatment-related factors have an important influence on the outcome of osseointegration procedures, it appears that anatomical factors may play an especially important role. Grafted bone appears to be more likely to permit osseointegration than local bone and integration is more likely in the mandible than in the maxilla.

H.3 Patient support group

Three surveys and a case series suggest that patients who are members of support groups derive benefits from their membership.^{23,24,102-104}

H.4 Patient education group

Patients who attended a monthly educational self-help group reported satisfaction with the group and suggested that they had a better understanding of cancer, of the views of patients and doctors and of reconstructive possibilities.¹⁰⁵ However, very few methodological details of this qualitative study were reported. Fourteen Swedish patients who attended a one-week psycho-educational programme a year after diagnosis appreciated all activities, learned new things, considered this knowledge useful and would recommend a week of rehabilitation in this format to other cancer patients.⁴⁷

H.5 Patient held records

The majority of respondents with head and neck cancer who were given a logbook, containing sections on communication and information, had read the whole logbook and said that it clarified things for them.¹⁰⁶ Respondents in a control group who were not given the logbook were more likely to have fear, anxiety, depression and tension, but there were no differences in the incidence of loneliness, insomnia, loss of control or reduction in self-esteem. The majority of professionals involved in treating patients who had received the logbook thought it was a good means of information-giving and it made a considerable contribution to the continuity of information. It was also useful in giving professionals an overview of the patient's case history and contributed to harmonising care between professionals.

I. Follow-up and recurrent disease

People who have been treated for UAT cancers remain at high risk, both of developing recurrent disease and of new cancers in the head and neck region and other parts of the body such as the lungs. Careful follow-up and systems for rapid referral for specialist assessment and treatment are therefore essential.

I.1 Routine follow-up

One systematic review that assessed 37 different strategies for following up patients treated for UAT cancer was identified.¹⁰⁷ These strategies were either common to all forms of UAT cancer (n=12) or specific to individual UAT cancers (n=25). Results were presented in terms of the number of times in a 5-year follow-up strategy an intervention was recommended. Cost information was reported, but differences in patients' outcomes were not presented. Every strategy recommended follow-up clinic consultations for detecting deterioration in the status of the patient. Chest X-rays were recommended by 10 of 12 general

strategies and 21 of 25 site-specific ones. Blood counts (7 of 12 general and 6 of 25 site-specific) and liver function tests (2 of 12 general and 11 of 25 site-specific) were the only other tests widely recommended.

The review reported few details about its methods or the included studies. The validity of contributing studies was not assessed, which could affect the validity of the review.

I.2 Imaging in the detection of recurrence

In a well-conducted diagnostic study that compared CT with MRI, both CT and MRI were found to have relatively low sensitivity (44–67% for CT and 56% for MRI) and moderate specificity (64–69% for CT and 78–83% for MRI) in detecting tumour recurrence and in distinguishing recurrence from post-radiation therapy changes.¹⁰⁸ However, MRI was found to be more accurate than CT (73–78% compared with 64%).

Two studies which compared CT with PET in patients with a suspected recurrence found that PET was more accurate than CT.^{109,110} A study which compared CT, PET and Colour-Doppler Echography (CDE) found that the accuracy of CT and CDE were comparable at 79% each, but the accuracy of PET was superior at 86%.¹¹¹ In a study which compared ultrasound with PET, PET was found to be more accurate than ultrasound (86% versus 64%).¹¹²

Overall the evidence reviewed consistently showed both MRI and PET to be more accurate than CT in detecting a recurrence of head and neck cancers. PET was also found to be more accurate than CT in patients where a recurrence was clinically suspected. The accuracy of CDE was found to be similar to that of CT. PET was also found to be more accurate than ultrasound.

J. Palliative interventions and care

Palliative care aims to maintain patients' comfort and dignity, and

primary care teams play an important role in providing such care. Whilst all professionals working with patients may address palliative care needs, palliative care specialists, working in hospitals, hospices or the community, are likely to be required to support patients with advanced disease.

As many as half of all patients with UAT cancers are likely to die of the disease eventually, and most will require palliative interventions; however, most of those treated for thyroid cancer enjoy good long-term health. For patients with late stage disease, good nursing care and palliative measures such as pain control and interventions to help them eat and breathe are crucial; those who are expected to live for a significant period may benefit from palliative surgery, radiotherapy or chemotherapy.

J.1 Palliative treatment

Evidence from one relatively small study suggests that chemotherapy, given in combination with radiotherapy, may significantly improve disease-free survival in previously untreated patients being treated palliatively for oropharyngeal cancers (Stages III to IV) in the short term. The complete response rate of patients treated by chemoradiotherapy was 39% higher than that of patients treated by radiotherapy alone. This difference was statistically significant ($p=0.015$).¹¹³ More research is required to assess longer-term benefits.

J.2 Assessment by a pain control service

One study was identified that assessed the services offered by a pain control service to terminally ill head and neck cancer patients undergoing palliative care.¹¹⁴ Patients were prescribed analgesia in accordance with the WHO pain control ladder. All patients were given regular medication; the 'as needed' approach was avoided. The main outcome measure relating to the intensity of pain used in the study was a Visual Analogue Scale (VAS). The mean VAS score (which has a maximum of 10) was 4.7 before analgesic therapy and 1.9 after initiation of therapy. This difference was

statistically significant ($p<0.001$). However, few patients completed the third recording of the VAS, intended to give longer-term results.

Since all patients were assessed by the pain control service, it is difficult to ascertain if the assessment had an effect on the outcome over and above the intervention that was decided upon by the service.

Appendix – research methods

This document presents a summary of a series of reviews undertaken by researchers at the Centre for Reviews and Dissemination (CRD), University of York. The review team constructed review questions in consultation with the editorial group and other experts in the field.

Comprehensive searches were carried out for each review question. Where appropriate, strategies were limited by methodological search filter or date. Searches were conducted for each question from a range of databases (MEDLINE, EMBASE, CancerLit, The Cochrane Library, Database of Abstracts of Reviews of Effects (DARE), AMED, HMIC databases (King's Fund database, DH-Data and HELMIS), CINAHL, British Nursing Index, NHS Economic Evaluation database (NHS EED) and SIGLE). Unpublished data were also identified through personal contact with researchers in the field. Two additional databases (Science Citation Index and Social Science Citation Index) were searched for one question each to assess their relevance to the review. However, it was found that their results did not yield any additional relevant studies over the other databases searched, so they were not used. Full details of the searches and strategies used are available from CRD (Tel: 01904 321846 or email: crd-info@york.ac.uk).

Literature searches were undertaken between October 2002 and April 2004.

Two reviewers screened titles and abstracts of all studies identified through electronic searching for relevance. Potentially eligible studies were retrieved in full and two reviewers selected studies. Selection of studies was based on pre-defined inclusion/exclusion criteria that specified for each question the participants, intervention,

comparator(s) and outcomes of interest. The same inclusion/exclusion criteria were applied to studies identified from non-electronic sources. Disagreements were resolved through discussion and any unresolved disagreements were discussed with a third reviewer. No restriction was made on publication language. Data were extracted from the included studies by one reviewer and checked for accuracy by another reviewer. However, some studies reported only as non-English language publications could not be data extracted (e.g. studies published in Japanese). Studies published in German, Dutch, Italian, Spanish and French were data extracted by one reviewer (sometimes it was only possible to extract minimal data owing to the language problems) and checked by a second reviewer.

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Effective Health Care

This bulletin is based on a series of systematic reviews carried out by the Centre for Reviews and Dissemination to inform the production of the guidance on head and neck cancer services.

Full details are provided in *Guidance on cancer services: improving outcomes in head and neck cancers: the manual and the research evidence* published by NICE. These may be obtained free of charge by calling the NHS Response Line on 0870 1555 455.

This bulletin was written and produced by staff at the Centre for Reviews and Dissemination, University of York.

The *Effective Health Care* bulletins are based on systematic review and synthesis of research on the clinical effectiveness, cost-effectiveness and acceptability of health service interventions. This is carried out by a research team using established methodological guidelines, with advice from expert consultants for each topic. Great care is taken to ensure that the work, and the conclusions reached, fairly and accurately summarise the research findings. The University of York accepts no responsibility for any consequent damage arising from the use of *Effective Health Care*.

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Effective Health Care Bulletins

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